

## REMARKS

This amendment is in response to the Official Action mailed April 21, 2005.

In the present paper, claim 4 has been amended. Claims 14-24 are withdrawn as directed to a non-elected invention, as a result of an earlier restriction requirement. Claims 1-13 are presently presented for the Examiner's consideration in view of the following remarks:

### *The Present Application*

The method and apparatus of the present invention permit the discrimination of molecules having similar molecular weights for detection and quantization using FT-ICR mass spectroscopy. The method may be performed in an FT-ICR MS chamber with little or no modification. The method permits on-line analysis of olefins and other compounds in hydrocarbon streams that also contain isomers of those compounds.

More specifically, the present invention makes use of a charge exchange reaction within the FT-ICR MS chamber to selectively ionize certain isomers of a compound while not ionizing others. In a charge exchange reaction, an ionic species reacts with a neutral species, wherein the neutral species is ionized and the ionic species is neutralized (present specification at [0044], lines 3-4). The energetics of a charge exchange reaction are a function of the difference in energy between the ionization potentials of the species involved (specification at [0044], lines 5-6). The charge exchange reaction is used by the inventor because the introduced ionic partner may be selected to have a very precise ionization potential. For example, ionized 1,2 difluorobenzene is used as the ionic partner in an example in the present specification because it has an ionization potential of 9.29 eV (see [0061] – [0066]). In the resulting charge exchange reaction with a mixed group of hydrocarbons, only aromatics, olefins and diolefins will form

ions and therefore be detected in the FT-ICR MS chamber, because members of those groups have ionization potentials below 9.29 eV (specification at [0048]).

The use of a charge exchange reaction to selectively ionize components of the sample mixture is an important advance over the prior art technique of modulating the electron energy of an electron impact source, as is done in the Llewellyn and Bomse references cited by the Examiner. While each atom or molecule of a given substance has substantially the same ionization potential due to the physical properties of the substance, electrons from an electron bombardment source have a relatively wide distribution of electron energy values. Although the mean energy value may be adjusted, the individual electrons vary in energy values. That condition means that, during impact ionization, some ions will be created from atoms or molecules having an ionization potential above the mean electron energy of the beam. In the present invention, that inaccuracy is eliminated because all ionic partner molecules or atoms have the same ionization potential, and the charge exchange reaction will occur only with species in the sample having ionization potentials below the precise ionization potential of the ionic partner.

A method according to the invention is claimed in claim 1, which is directed to a method for identifying components of a sample mixture in a Fourier transform ion cyclotron resonance mass spectrometer (FT-ICR MS) having a FT-ICR MS chamber. The components of the sample mixture have respective ionization potentials defining a range of ionization potentials. The method includes the steps of selecting a first ionic partner having an ionization potential within the range of ionization potentials, introducing the first ionic partner into the FT-ICR MS chamber, introducing the sample mixture into the FT-ICR MS chamber. A charge exchange reaction takes place in the chamber between the first ionic partner and those components of the

sample mixture having ionization potentials below the ionization potential of the first ionic partner, forming a first ionized mixture. The ionized components of the first ionized mixture are then detected in the FT-ICR MS chamber.

The Examiner has rejected claims 1, 4-7 and 11 under 35 U.S.C. § 102(b) as anticipated by U.S. Patent No. 5,015,848 to Bomse et al. ("Bomse"). Additionally, the Examiner has rejected claims 2-3, 8-9 and 13 under 35 U.S.C. § 103(a) as unpatentable over Bomse, and has rejected claims 1-2, 4-8, 10 and 12 as unpatentable over U.S. Patent No. 3,446,957 to Llewellyn et al. ("Llewellyn") in view of U.S. Patent No. 3,937,955 to Comisarow et al. ("Comisarow").

#### *The Bomse Patent*

Bomse is directed to a method and apparatus for mass spectrometric analysis wherein the electron energy of an electron impact ionization source is modulated (Bomse, col. 5, lines 66-68). The modulation conditions are chosen such that the threshold for ionization of at least one species in the analyte falls within the bounds of the modulated electron energy (col. 6, lines 1-5). Bomse further discloses using Fourier transforms for interpreting the results.

As discussed above, the technique suffers from the inherent inaccuracies presented by using an electron beam having a distribution of electron energies to define a theoretically discrete threshold.

#### *The Llewellyn Patent*

Like Bomse, Llewellyn discloses an ion cyclotron spectrometer using an ion beam that is scanned over a range of beam ionization potentials (Llewellyn, abstract, col. 2, lines 31-33).

*The Comisarow Patent*

Comisarow teaches the use of Fourier transforms to convert the results of an ion cyclotron resonance spectroscope to the frequency domain for analysis (Comisarow, abstract).

*Claim 1*

Claim 1 has been rejected by the Examiner as anticipated by Bomse and as obvious over Llewellyn in view of Comisarow. Applicant respectfully submits that claim 1 is patentable over those references because the references, individually or in combination, do not teach or suggest each of the limitations contained in claim 1. Specifically, Applicant submits that the following elements of claim 1 are not taught or suggested in the cited art:

“selecting a first ionic partner having an ionization potential within the range of ionization potentials”

The Examiner has identified the electron beams of Bomse and of Llewellyn as teaching the first ionic partner of Claim 1. Applicant respectfully submits that an electron beam cannot have an “ionization potential” as required by claim 1. “Ionization potential,” as that special term is exclusively used in the art, is a discrete and exact amount of energy required to remove an electron from an isolated atom or molecule (see, e.g., Encyclopaedia Britannica Online, summary article “Ionization Potential,” found at [www.britannica.com](http://www.britannica.com) and appended hereto). An atom or a molecule may be ionized by removing its outermost electron, giving the atom or molecule a charge of +1. In contrast, a dissociated electron cannot be “ionized” under any meaning of that term. Put another way, it makes no sense to remove an electron from an

electron, and no ionization potential may be measured for removing an electron from an electron.

An electron therefore cannot have an “ionization potential,” as required by claim 1.

The step of selecting an ionic partner in claim 1 is based on ionization potential. As discussed above, the ionization potential is a precise value, and is the value for each and every molecule of the ionic partner. That precision results in the precision of the inventive spectroscopy method. In contrast, Bomse and Llewellyn rely on the energy imparted to electrons in an electron beam to establish an ionization threshold in the chamber. That energy is an average energy, with individual electrons having a range of energies, resulting in the ionization of particles having a range of ionization potentials.

“introducing the sample mixture into the FT-ICR MS chamber, whereby a charge exchange reaction takes place in the chamber between the first ionic partner and those components of the sample mixture having ionization potentials below the ionization potential of the first ionic partner, forming a first ionized mixture”

Claim 1 requires that a charge exchange reaction take place between the first ionic partner and components in the sample mixture. The Examiner alleges that a charge exchange reaction is taught by the electron beam ionization of the sample mixture in Bomse (col. 6, lines 58-68) and Llewellyn (col. 1, lines 19-23).

The term “charge exchange reaction” is precisely defined in the specification of the present application; that definition being based on common usage of that term in the art:

In a charge exchange reaction, an ionic reagent having an ionization potential  $x$  is associated with a sample compound having an ionization potential  $y$  where  $x > y$ . Because the energy released by neutralizing the reagent is greater than the energy

required to ionize the sample, the reaction is exothermic. In a sample containing compounds having various ionization potentials, compounds that have an ionization potential greater than  $x$  are not ionized.

Specification at [0019]. Applicant has defined “charge exchange reaction” in his specification, and that term must be so interpreted in the claims. Further, that definition is the plain meaning given the term by those skilled in the art.

Under the definition set forth in the specification, the reagent is neutralized in the reaction. Stated another way, the plain meaning of “charge exchange reaction” is that the charge is “exchanged”: the ionic reagent becomes neutralized, and the neutral compound becomes charged. No such exchange can be said to take place in the electron bombardment ionization that takes place in Bomse and Llewellyn. Instead, the free electrons collide with molecules and impart their energy, but electrons do not and cannot become “neutralized,” as is required by the definition of “charge exchange reaction” set forth in the present specification.

Further, the ionic reagent in a charge exchange reaction (as that term is used in the present application and in common usage) must have an ionization potential. As noted above, a dissociated electron cannot have an ionization potential. The ionization taking place in Bomse and Llewellyn therefore cannot be termed a “charge exchange reaction.”

The Applicant therefore respectfully submits that claim 1 is patentable over the art cited by the Examiner at least because that art does not teach or suggest “a first ionic partner having an ionization potential,” and does not teach or suggest a “charge exchange reaction” as that term is defined in the specification and in common usage. Applicant further submits that claims 2-13,

which depend directly or indirectly from claim 1 and incorporate the limitations of claim 1, are patentable for at least the same reasons.

*Claims 3 and 9*

Claim 3 was rejected by the Examiner as obvious over Bomse because “it would have been obvious to incorporate any of the ionized gases because Bomse et al. teach the analysis can measure any mixture (see col. 3, lines 1-9).” Applicant respectfully disagrees with the Examiner’s analysis.

Claim 3 requires that the first ionic partner is selected from the group consisting of pyridine, nitrogen oxide and 1,2 difluorobenzene. In rejecting claim 1, the Examiner characterizes the electron beam from the electron impact ionization source of Bomse as the first ionic partner (Bomse, col. 5, line 66 – col. 6, line 9). If the first ionic partner is the electron beam, it cannot be one of the compounds recited in claim 3.

The Examiner cites as support for the rejection a passage at col. 3, lines 1-9 of Bomse. That passage suggests that the Bomse device be applied to “measurements of novel, previously unknown species.” The Examiner concludes that the compounds of claim 3 would fall within that scope. Applicant points out that Bomse suggests that previously unknown species be measured, Bomse does not teach or suggest replacing the electron beam (which the Examiner alleges is the ionic partner) with anything.

Finally, it would not be practical to substitute the compounds listed in claim 3 for the electrons of Bomse, and to then modulate their energy, as would be required by the teachings of Bomse.

For each of those additional reasons, Applicant respectfully submits that claim 3 is patentable over Bomse. Further, claim 9, which contains similar limitations regarding the second ionic partner, is patentable for the same reasons.

*Claim 4*

Claim 4 has been amended to require that the step of introducing a first ionic partner comprises producing the first ionic partner by bombarding a neutral reagent gas with electrons within the chamber. The Examiner has argued that that step is anticipated in Bomse by an electron impact ionizer used for generating time variant ionization of components of the analyte (at col. 4, lines 25-43).

Applicant respectfully submits that, while the structure identified by the Examiner does indeed produce ions, it does not produce the first ionic partner, as required by claim 4. Instead, it produces ions of the analyte, which are then mass filtered, detected and processed (col. 4, lines 27-35).

The electron beam, which the Examiner has identified as the first ionic partner in Bomse, is not produced in the chamber and is not produced by bombarding a neutral reagent gas with electrons, as required by claim 4.

Applicant therefore submits that claim 4 is patentable over the cited art for that additional reason.

*Conclusion*


Applicant therefore assert that claims 1-13 are now in condition for allowance, and earnestly requests that the Examiner issue a Notice of Allowance.



Should the Examiner have any questions regarding the present case, the Examiner should not hesitate in contacting the undersigned at the number provided below.

Respectfully,

By



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